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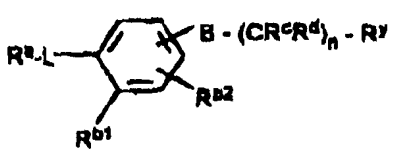
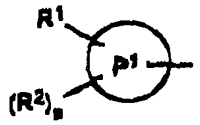
(54) Title: (HETERO)ARYL CARBOXAMIDE DERIVATIVES, PROCESS FOR THEIR PREPARATION AND THEIR USE IN THE TREATMENT OF CNS DISORDERS

(57) Abstract

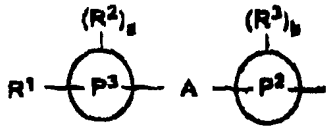
Compounds of formula (I), processes for their preparation and their use as CNS agents are disclosed, in which R^a is a group of formula (i), in which P^1 is bicyclic aryl, a bicyclic heterocyclic ring containing 1 to 3 heteroatoms selected from oxygen, nitrogen and sulphur; or R^a is a group of formula (ii), wherein P^2 and P^3 are independently phenyl, bicyclic aryl, a 5– to 7–membered heterocyclic ring containing 1 to 3 heteroatoms selected from oxygen, nitrogen and sulphur, or a bicyclic heterocyclic group containing 1 to 3 heteroatoms selected from oxygen, nitrogen or sulphur providing that at least one of P^2 and P^3 is a bicyclic aryl or bicyclic heterocyclic group; A is a bond or oxygen, $S(O)_m$ where m is 0 to 2, carbonyl, or CH_2 or NR^4; L is a group of formula –C(=V)–DG – or –DG–C(=V)–; V is oxygen or sulphur; D is nitrogen, carbon or a CH group, G is hydrogen or C_{1-6}alkyl, providing that D is nitrogen or a CH group, or G together with R^{b1} forms a group W where W is $(CR^{16}R^{17})_t$ or $(CR^{16}R^{17})_u$–j where u is 0, 1, 2 or 3 and J is oxygen, sulphur, $CR^{16}=CR^{17}$, $CR^{16}=N$, $=CR^{16}O$, $=CR^{16}S$ or $=CR^{16}–NR^{17}$; B is oxygen, S(O)p where p is 0, 1 or 2, NR^6 where R^6 is hydrogen or C_{1-6}alkyl or B is $CR^7=CR^8$ where R^7 and R^8 are independently hydrogen or C_{1-6}alkyl; R^c and R^d are independently hydrogen or C_{1-6}alkyl; R^y is a 5– to 7–membered heterocyclic ring containing 1 to 3 heteroatoms selected from oxygen, nitrogen and sulphur, or R^y is a group of formula $–NR^eR^f$.



(I)



(i)



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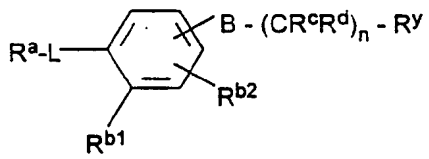
(HETERO)ARYL CARBOXAMIDE DERIVATIVES, PROCESS FOR THEIR PREPARATION AND THEIR USE IN THE TREATMENT OF CNS DISORDERS

The present invention relates to novel urea derivatives processes for their preparation, and pharmaceutical compositions containing them.

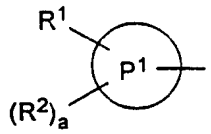
WO 95/15954, WO 95/17398, WO 95/26328 and WO 96/06079 disclose a series of piperazine derivatives which are said to possess $5HT_{1D}$ receptor antagonist activity. These compounds are alleged to be of use in the treatment of various CNS disorders such as depression. EPA 0533266/7/8 disclose a series of benzanilide derivatives which are said to possess 5-HT_{1D} receptor antagonist activity.

A structurally distinct class of compounds have now been found to exhibit combined $5HT_{1A}$, $5HT_{1B}$ and $5HT_{1D}$ receptor antagonist activity. It is expected that such compounds will be useful for the treatment and prophylaxis of various CNS disorders with the advantage of a relatively fast onset of action. In a first aspect, the present invention therefore provides a compound of formula (I) or a salt thereof:



(I)

in which R^a is a group of formula (i)



(i)

in which P^1 is bicyclic aryl, a bicyclic heterocyclic ring containing 1 to 3 heteroatoms selected from oxygen, nitrogen and sulphur;

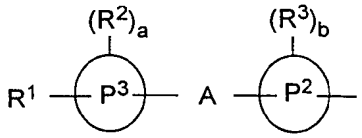
R^1 is hydrogen, halogen, C_{1-6}alkyl, C_{3-6}cycloalkyl, COC_{1-6}alkyl, C_{1-6}alkoxy, hydroxy, hydroxyC_{1-6}alkyl, hydroxyC_{1-6}alkoxy, C_{1-6}alkoxyC_{1-6}alkoxy, C_{1-6}alkanoyl, nitro, trifluoromethyl, cyano, SR^9, SOR^9, SO_2R^9, $SO_2NR^{10}R^{11}$, CO_2R^{10}, $CONR^{10}R^{11}$, $CO_2NR^{10}R^{11}$, $CONR^{10}(CH_2)_cCO_2R^{11}$, $(CH_2)_cNR^{10}R^{11}$,

$(CH_2)_cCONR^{10}R^{11}$, $(CH_2)_cNR^{10}COR^{11}$, $(CH_2)_cCO_2C_{1-6}$alkyl, $CO_2(CH_2)_cOR^{10}$, $NR^{10}R^{11}$, $NR^{10}CO_2R^{11}$, $NR^{10}CONR^{10}R^{11}$, $CR^{10}=NOR^{11}$, $CNR^{10}=NOR^{11}$, where R^9, R^{10} and R^{11} are independently hydrogen or C_{1-6}alkyl and c is 1 to 4;

R^2 is hydrogen, halogen, C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{3-6}cycloalkenyl, C_{1-6}alkoxy, C_{1-6}alkanoyl, aryl, acyloxy, hydroxy, nitro, trifluoromethyl, cyano, CO_2R^{10}, $CONR^{10}R^{11}$, $NR^{10}R^{11}$ where R^{10} and R^{11} are as defined for R^1;

a is 1, 2 or 3;

or R^a is a group of formula (ii)



(ii)

wherein P^2 and P^3 are independently phenyl, bicyclic aryl, a 5- to 7- membered heterocyclic ring containing 1 to 3 heteroatoms selected from oxygen, nitrogen and sulphur, or a bicyclic heterocyclic group containing 1 to 3 heteroatoms selected from oxygen, nitrogen or sulphur providing that at least one of P^2 and P^3 is a bicyclic aryl or bicyclic heterocyclic group;

A is a bond or oxygen, $S(O)_m$ where m is 0 to 2, carbonyl, or CH_2 or NR^4 where R^4 is hydrogen or C_{1-6}alkyl;

R^1 is as defined above for formula (i) or is a 5 to 7-membered heterocyclic ring, containing 1 to 3 heteroatoms selected from oxygen, nitrogen or sulphur, optionally substituted by C_{1-6}alkyl, halogen or C_{1-6} alkanoyl;

R^2 and R^3 are independently hydrogen, halogen, C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{3-6}cycloalkenyl, C_{1-6}alkoxy, C_{1-6}alkanoyl, aryl, acyloxy, hydroxy, nitro, trifluoromethyl, cyano, CO_2R^{10}, $CONR^{10}R^{11}$, $NR^{10}R^{11}$ where R^{10} and R^{11} are as defined for R^1;

and a and b are independently 1, 2 or 3;

L is a group of formula

- C (=V) - DG - or - DG - C (=V) -

V is oxygen or sulphur;

D is nitrogen, carbon or a CH group, G is hydrogen or C_{1-6}alkyl, providing that D is nitrogen or a CH group, or G together with R^{b1} forms a group W where W is $(CR^{16}R^{17})_t$ where t is 2, 3 or 4 and R^{16} and R^{17} are independently hydrogen or C_{1-6}alkyl or W is $(CR^{16}R^{17})_u$-J where u is 0, 1, 2 or 3 and J is oxygen, sulphur, $CR^{16}=CR^{17}$, $CR^{16}=N$, $=CR^{16}O$, $=CR^{16}S$ or $=CR^{16}-NR^{17}$;

B is oxygen, S(O) p where p is 0, 1 or 2, NR^6 where R^6 is hydrogen or C_{1-6}alkyl or B is $CR^7=CR^8$ where R^7 and R^8 are independently hydrogen or C_{1-6}alkyl;

R^c and R^d are independently hydrogen or C_{1-6}alkyl;

R^y is a 5- to 7-membered heterocyclic ring containing 1 to 3 heteroatoms selected from oxygen, nitrogen and sulphur, or R^y is a group of formula - NR^eR^f in which R^e and R^f are independently hydrogen, C_{1-6}alkyl, or aralkyl;

R^{b1} and R^{b2} are independently hydrogen, halogen, hydroxy, C_{1-6}alkyl, trifluoromethyl, C_{1-6}alkoxy or aryl, or R^{b1} together with G forms a group W as defined above; and

n is 1 to 4.

C_{1-6}alkyl groups whether alone or as part of another group may be straight chain or branched. The term 'acyloxy' is used herein to describe a group -$OC(O)C_{1-6}$alkyl. The term 'aryl' is used herein to describe, unless otherwise stated, a group such as phenyl. The term 'aralkyl' is used herein to describe, unless otherwise stated, a group such as benzyl.

The bicyclic aryl group represented by P^1, P^2 and/or P^3, which may be partially saturated, is preferably naphthyl.

Examples of bicyclic heterocyclic rings containing 1 to 3 heteroatoms selected from oxygen, nitrogen and sulphur include quinoline, isoquinoline, indole, benzofuran and benzothiophene rings. The heterocyclic groups can be linked to the remainder of the molecule via a carbon atom or, when present, a suitable nitrogen atom.

Examples of 5 to 7 membered heterocyclic rings containing 1 to 3 heteroatoms selected from oxygen, nitrogen and sulphur represented by P^1, P^2 and/or P^3, include thienyl, furyl, pyrrolyl, triazolyl, imidazolyl, oxazolyl, thiazolyl, oxadiazolyl, isothiazolyl, isoxazolyl, thiadiazolyl, pyrimidyl and pyrazinyl, preferably pyridyl.

R^1 is preferably a halogen atom for example, fluorine, chlorine or bromine, and R^2 and/or R^3 are each preferably hydrogen, halogen for example a chloro group or a C_{1-6}alkyl group for example a methyl group.

a and b are each preferably 1 or 2.

A is preferably a bond or oxygen.

In the group L, as defined above:-

V is preferably oxygen.

D is preferably nitrogen and G is preferably a hydrogen atom or together with R^{b1} forms group W, preferably $-(CH_2)_2-$.

R^{b1} and R^{b2} are preferably hydrogen or a halogen atom for example chlorine or iodine, or a C_{1-6}alkoxy group for example methoxy , or R^{b1} together with G forms group W referred to above.

B is preferably oxygen.

R^c and R^d are preferably hydrogen.

R^y is preferably a dialkylamino(e.g. dimethylamino) group.

n is preferably 2.

Preferably the group $B-(CR^cR^d)_n-R^y$ has a meta relationship with respect to the group R^aL. Preferably the group R^{b2} has a para relationship with respect to the group R^aL.

Particularly preferred compounds according to the invention include:-

N-[3-(2-dimethylaminoethoxy)-4-iodophenyl]naphth-1-ylcarboxamide

N-[3-(2-dimethylaminoethoxy)-4-iodophenyl]quinolin-4-ylcarboxamide

or pharmaceutically acceptable salts thereof.

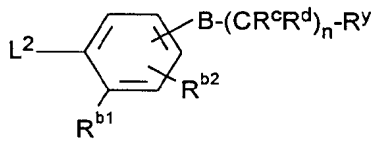
Preferred salts of the compounds of formula (I) are pharmaceutically acceptable salts. These include acid addition salts such as hydrochlorides, hydrobromides, phosphates, acetates, fumarates, maleates, tartrates, citrates, oxalates, methanesulphonates and p-toluenesulphonates.

Certain compounds of formula (I) are capable of existing in stereoisomeric forms. It will be understood that the invention encompasses all geometric and optical isomers of the compounds of formula (I) and the mixtures thereof including racemates.

Compounds of the invention can be prepared using procedures known in the art. In a further aspect the present invention provides a process for the preparation of a compound of formula (I) or a pharmaceutically acceptable salt thereof which comprises coupling a compound of formula (II):

$$Ra\text{-}L^1 \qquad (II)$$

with a compound of formula (III).



(III)

in which R^a, R^{b1}, R^{b2}, R^c, Rd, Ry, B and n are as defined in formula (I) and L^1 and L^2 contain the appropriate functional groups which are capable of reacting together to form the L moiety;

and optionally thereafter:

- removing any protecting groups,
- converting a compound of formula (I) into another compound of formula (I),
- forming a pharmaceutically acceptable salt.

In the reaction of the compounds of formulae (II) and (III), suitable examples of groups L^1 and L^2 include:-

L^1 is COL^a and L^2 is NH_2

L^1 is NH_2 and L^2 is COL^a

in which L^a is an appropriate leaving group.

Suitably one of L^1 and L^2 is an activated carboxylic acid derivative such as an acyl chloride or acid anhydride,and the other is an amine group.Activated compounds of formulae(II) and (III) can also be prepared by reaction of the corresponding carboxylic acid with a coupling agent such as dicyclohexylcarbodiimide,carbonyldiimidazole or diphenylphosphorylazide. Preferably L^1 or L^2 is a group COL^a where L^a is halo particularly chloro.

Compounds of formulae(II) and (III) are typically reacted together in an inert solvent such as dimethylformamide,tetrahydrofuran or dichloromethane at ambient or

elevated temperature in the presence of a base such as an alkali metal hydroxide,trimethylamine or pyridine.

Compounds of formula (I) can be converted into further compounds of formula (I) using standard techniques.

Intermediate compounds of formulae (II) and (III) can be prepared using standard procedures known in the art.

It will be appreciated to those skilled in the art that it may be necessary to protect certain reactive substituents during some of the above procedures. Standard protection and deprotection techniques can be used. For example, primary amines can be protected as phthalimide, benzyl, benzyloxycarbonyl or trityl derivatives. These groups can be removed by conventional procedures well known in the art.

Carboxylic acid groups can be protected as esters. Aldehyde or ketone groups can be protected as acetals, ketals, thioacetals or thioketals. Deprotection is achieved using standard conditions.

$5HT_{1A/1B/1D}$ receptor antagonists, and in particular the compounds of the present invention, are expected to be of use in the treatment of CNS disorders such as mood disorders, including depression, seasonal affective disorder and dysthymia; anxiety disorders, including generalised anxiety, panic disorder, agoraphobia, social phobia, obsessive compulsive disorder and post-traumatic stress disorder; memory disorders, including dementia, amnestic disorders and age-associated memory impairment; disorders of eating behaviours, including anorexia nervosa and bulimia nervosa ;and sleep disorders. Other CNS disorders include motor disorders such as Parkinson's disease, dementia in Parkinson's disease, neuroleptic-induced Parkinsonism and tardive dyskinesias, as well as other psychiatric disorders.

$5HT_{1A/1B/1D}$ receptor antagonists, and in particular compounds of the present invention, may also be of use in the treatment of endocrine disorders such as hyperprolactinaemia, in the treatment of vasospasm (particularly in the cerebral vasculature) and hypertension, as well as disorders in the gastrointestinal tract where changes in motility and secretion are involved. They may also be of use in the treatment of sexual dysfunction and hypothermia.

The present invention also provides a compound of general formula (I) or a physiologically acceptable salt or solvate thereof for use in the treatment of the aforementioned disorders.

In a further aspect the invention provides a method of treating the aforementioned disorders which comprises administering an effective amount to a patient in need of such treatment of a compound of general formula (I) or a pharmaceutically acceptable salt or solvate thereof.

In particular the invention provides a compound of general formula (I) or a physiologically acceptable salt or solvate thereof for use in the treatment or prophylaxis of depression.

It will be appreciated by those skilled in the art that the compounds according to the invention may advantageously be used in conjunction with one or more other therapeutic agents, for instance, different antidepressant agents.

The present invention also provides a pharmaceutical composition, which comprises a compound of formula (I) or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

A pharmaceutical composition of the invention, which may be prepared by admixture, suitably at ambient temperature and atmospheric pressure, is usually adapted for oral, parenteral or rectal administration and, as such, may be in the form of tablets, capsules, oral liquid preparations, powders, granules, lozenges, reconstitutable powders, injectable or infusible solutions or suspensions or suppositories. Orally administrable compositions are generally preferred.

Tablets and capsules for oral administration may be in unit dose form, and may contain conventional excipients, such as binding agents, fillers, tabletting lubricants, disintegrants and acceptable wetting agents. The tablets may be coated according to methods well known in normal pharmaceutical practice.

Oral liquid preparations may be in the form of, for example, aqueous or oily suspension, solutions, emulsions, syrups or elixirs, or may be in the form of a dry product for reconstitution with water or other suitable vehicle before use. Such liquid preparations may contain conventional additives such as suspending agents, emulsifying agents, non-aqueous vehicles (which may include edible oils), preservatives, and, if desired, conventional flavourings or colorants.

For parenteral administration, fluid unit dosage forms are prepared utilising a compound of the invention or pharmaceutically acceptable salt thereof and a sterile vehicle. The compound, depending on the vehicle and concentration used, can be either suspended or dissolved in the vehicle. In preparing solutions, the compound can be

dissolved for injection and filter sterilised before filling into a suitable vial or ampoule and sealing. Advantageously, adjuvants such as a local anaesthetic, preservatives and buffering agents are dissolved in the vehicle. To enhance the stability, the composition can be frozen after filling into the vial and the water removed under vacuum. Parenteral suspensions are prepared in substantially the same manner, except that the compound is suspended in the vehicle instead of being dissolved, and sterilisation cannot be accomplished by filtration. The compound can be sterilised by exposure to ethylene oxide before suspension in a sterile vehicle. Advantageously, a surfactant or wetting agent is included in the composition to facilitate uniform distribution of the compound.

The composition may contain from 0.1% to 99% by weight, preferably from 10 to 60% by weight, of the active material, depending on the method of administration.

The dose of the compound used in the treatment of the aforementioned disorders will vary in the usual way with the seriousness of the disorders, the weight of the sufferer, and other similar factors. However, as a general guide suitable unit doses may be 0.05 to 1000 mg, more suitably 1.0 to 200 mg, and such unit doses may be administered more than once a day, for example two or three a day. Such therapy may extend for a number of weeks or months.

The following Examples illustrate the preparation of compounds of the invention.

Example 1

N-[3-(2-Dimethylaminoethoxy)-4-iodophenyl]naphth-1-ylcarboxamide

Under an atmosphere of argon, a stirred suspension of 1-napthoic acid (150mg, 0.87mmole) in dichloromethane was stirred with oxalyl chloride (0.30ml) and DMF (1 drop) for 2h. The solution was concentrated *in vacuo* to afford a gum, which was azeotroped with toluene to remove residual oxalyl chloride. The gum was dissolved in dichloromethane (20ml) under argon and treated with 3-(2-dimethylaminoethoxy-4-iodoaniline (266mg, 0.87 mmole, D50 in WO 95/15954) and triethylamne (0.4ml). The reaction mixture was stirred at room temperature for 2h, then treated with aqueous K_2CO_3 and the organic layer separated, dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by silica gel chromatography eluting with 3% methanol/dichloromethane to afford the title compound (100mg, 25%).

^{1}H NMR (250MHz, $CDCl_3$) δ(ppm): 8.29 (s, 1H), 8.15 (m, 1H), 7.8 - 7.7 (m, 2H), 7.6 - 7.33 (m, 4H), 7.4 (m, 2H), 6.75 (d, 1H), 4.0 (m, 2H), 2.7 (m, 2H), 2.25 (s, 6H).

Example 2

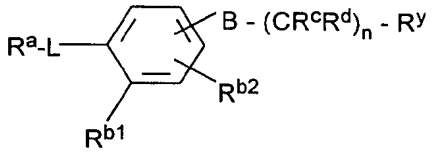
N-[3-(2-Dimethylaminoethoxy)-4-iodophenyl]quinolin-4-ylcarboxamide

The title compound was prepared from quinoline-4-carboxylic acid and 3-(2-dimethylaminoethoxy)-4-iodoaniline (D50 in WO 95/15954) following a similar procedure to Example 1.

^{1}H NMR (250MHz, $CDCl_3$) δ (ppm): 8.88 (s, 1H), 8.69 (d, 1H), 8.13 (d, 1H), 8.01 (d, 1H), 7.58 (m, 2H), 7.53 (m, 2H), 7.34 (d, 1H), 7.05 - 7.02 (m, 1H), 4.17 (t, 2H), 2.87 (t, 2H), 2.41 (s, 6H).

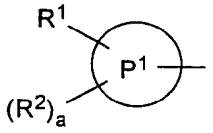
CLAIMS

1. A compound of formula (I) or a salt thereof:



(I)

in which R^a is a group of formula (i)



(i)

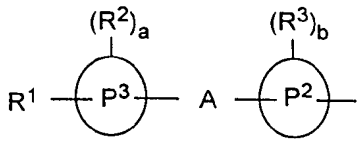
in which P^1 is bicyclic aryl, a bicyclic heterocyclic ring containing 1 to 3 heteroatoms selected from oxygen, nitrogen and sulphur;

R^1 is hydrogen, halogen, C_{1-6}alkyl, C_{3-6}cycloalkyl, COC_{1-6}alkyl, C_{1-6}alkoxy, hydroxy, hydroxyC_{1-6}alkyl, hydroxyC_{1-6}alkoxy, C_{1-6}alkoxyC_{1-6}alkoxy, C_{1-6}alkanoyl, nitro, trifluoromethyl, cyano, SR^9, SOR^9, SO_2R^9, $SO_2NR^{10}R^{11}$, CO_2R^{10}, $CONR^{10}R^{11}$, $CO_2NR^{10}R^{11}$, $CONR^{10}(CH_2)_cCO_2R^{11}$, $(CH_2)_cNR^{10}R^{11}$, $(CH_2)_cCONR^{10}R^{11}$, $(CH_2)_cNR^{10}COR^{11}$, $(CH_2)_cCO_2C_{1-6}$alkyl, $CO_2(CH_2)_cOR^{10}$, $NR^{10}R^{11}$, $NR^{10}CO_2R^{11}$, $NR^{10}CONR^{10}R^{11}$, $CR^{10}{=}NOR^{11}$, $CNR^{10}{=}NOR^{11}$, where R^9, R^{10} and R^{11} are independently hydrogen or C_{1-6}alkyl and c is 1 to 4;

R^2 is hydrogen, halogen, C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{3-6}cycloalkenyl, C_{1-6}alkoxy, C_{1-6}alkanoyl, aryl, acyloxy, hydroxy, nitro, trifluoromethyl, cyano, CO_2R^{10}, $CONR^{10}R^{11}$, $NR^{10}R^{11}$ where R^{10} and R^{11} are as defined for R^1;

a is 1, 2 or 3;

or R^a is a group of formula (ii)



(ii)

wherein P^2 and P^3 are independently phenyl, bicyclic aryl, a 5- to 7- membered heterocyclic ring containing 1 to 3 heteroatoms selected from oxygen, nitrogen and sulphur, or a bicyclic heterocyclic group containing 1 to 3 heteroatoms selected from oxygen, nitrogen or sulphur providing that at least one of P^2 and P^3 is a bicyclic aryl or bicyclic heterocyclic group;

A is a bond or oxygen, $S(O)_m$ where m is 0 to 2, carbonyl, or CH_2 or NR^4 where R^4 is hydrogen or C_{1-6}alkyl;

R^1 is as defined above for formula (i) or is a 5 to 7-membered heterocyclic ring, containing 1 to 3 heteroatoms selected from oxygen, nitrogen or sulphur, optionally substituted by C_{1-6}alkyl, halogen or C_{1-6} alkanoyl;

R^2 and R^3 are independently hydrogen, halogen, C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{3-6}cycloalkenyl, C_{1-6}alkoxy, C_{1-6}alkanoyl, aryl, acyloxy, hydroxy, nitro, trifluoromethyl, cyano, CO_2R^{10}, $CONR^{10}R^{11}$, $NR^{10}R^{11}$ where R^{10} and R^{11} are as defined for R^1;

and a and b are independently 1, 2 or 3;

L is a group of formula

- C (=V) - DG - or - DG - C (=V) -

V is oxygen or sulphur;

D is nitrogen, carbon or a CH group, G is hydrogen or C_{1-6}alkyl, providing that D is nitrogen or a CH group, or G together with R^{b1} forms a group W where W is $(CR^{16}R^{17})_t$ where t is 2, 3 or 4 and R^{16} and R^{17} are independently hydrogen or C_{1-6}alkyl or W is $(CR^{16}R^{17})_u$-J where u is 0, 1, 2 or 3 and J is oxygen, sulphur, $CR^{16}=CR^{17}$, $CR^{16}=N$, $=CR^{16}O$, $=CR^{16}S$ or $=CR^{16}-NR^{17}$;

B is oxygen, S(O) p where p is 0, 1 or 2, NR^6 where R^6 is hydrogen or C_{1-6}alkyl or B is $CR^7=CR^8$ where R^7 and R^8 are independently hydrogen or C_{1-6}alkyl;

R^c and R^d are independently hydrogen or C_{1-6}alkyl;

R^y is a 5- to 7-membered heterocyclic ring containing 1 to 3 heteroatoms selected from oxygen, nitrogen and sulphur, or R^y is a group of formula - NR^eR^f in which R^e and R^f are independently hydrogen, C_{1-6}alkyl, or aralkyl;

R^{b1} and R^{b2} are independently hydrogen, halogen, hydroxy, C_{1-6}alkyl, trifluoromethyl, C_{1-6}alkoxy or aryl, or R^{b1} together with G forms a group W as defined above; and n is 1 to 4.

2. A compound according to claim 1 in which R^1 is a halogen atom.

3. A compound according to claim 1 or 2 in which R^2 and/or R^3 are each hydrogen, halogen or a C_{1-6} alkyl group.

4. A compound according to any of the preceding claims in which one of P^1, P^2 and/or P^3 is a naphthyl group.

5. A compound according to any of the preceding claims in which V is oxygen.

6. A compound according to any of the preceding claims in which D is nitrogen and G is hydrogen.

7. A compound according to any of the preceding claims in which R^{b1} and R^{b2} are hydrogen or halogen,or R^{b1} together with G forms a $-(CH_2)_2-$ group.

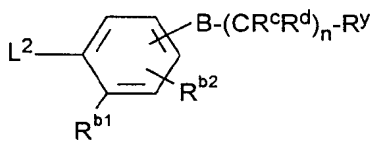
8. A compound according to any of the preceding claims in which R^y is a dialkylamino group.

9. A compound according to claim 1 which is:
N-[3-(2-dimethylaminoethoxy)-4-iodophenyl]naphth-1-ylcarboxamide
N-[3-(2-dimethylaminoethoxy)-4-iodophenyl]quinolin-4-ylcarboxamide
or a pharmaceutically acceptable salt thereof.

10. A process for the preparation of a compound of formula (I) according to claim 1 or a pharmaceutically salt thereof which comprises coupling a compound of formula (II):

$$Ra\text{-}L^1 \qquad (II)$$

with a compound of formula (III).



(III)

in which R^a, R^{b1}, R^{b2}, R^c, R^d, R^y, B and n are as defined in formula (I) and L^1 and L^2 contain the appropriate functional groups which are capable of reacting together to form the L moiety;

and optionally thereafter:

- removing any protecting groups,
- converting a compound of formula (I) into another compound of formula (I),
- forming a pharmaceutically acceptable salt.

11. A compound according to any of claims 1 to 9 for use in therapy.

12. A pharmaceutical composition which comprises a compound according to any of claims 1 to 9 and a pharmaceutically acceptable carrier.